

1. (Amended) A method for the detection of an analyte in a sample, which comprises contacting the sample to be tested with a three-dimensional array comprising a polydiacetylene backbone and a substrate, wherein the substrate has direct affinity for an analyte or is capable of binding to an analyte or is capable of reacting with an analyte; and wherein said analyte, when present, leads to a change in fluorescence of said polydiacetylene backbone;

and detecting the change in fluorescence to indicate the presence of an analyte.

11. (Amended) The method of claim 10 wherein the array is in the form of a solution of a liposome or tubule.

### **REMARKS**

Claims 1-46 are now in the application. Claims 1-19 are directed to the elected invention. Claims 20-46 are drawn to non-elected inventions and may be cancelled by the Examiner upon the allowance of the claims directed to the elected invention.

Claim 1 has been amended for purposes of clarification and not to limit the scope thereof. Claim 11 has been amended to now depend from Claim 10 thereby addressing the objection to Claim 11. Attached are replacement pages 38, 39 and 40 to delete the large blank spaces on these pages as requested by the Examiner. This addresses the objections raised by the Examiner with respect to Claims 9-10, 15-16 and 18-19.

Also as requested by the examiner is another Information Disclosure Statement.

The rejection of Claims 1-19 under 35 USC §112, second paragraph has been overcome by the amendments to the claims and/or are not deemed tenable. In particular, the claims no longer recite the term "incorporated in the array". In addition, Claim 1 now recites "is capable of binding" in place of the term "can function as a binder" and also recites "is capable of reacting" in place of "can react". Claim 1 has also been amended to clarify that an analyte leads to a change in fluorescence of the polydiacetylene backbone.

With respect to the Examiner criticism of the terms “direct affinity” and “binder” such term are readily understandable by those skilled in the art and therefore are not indefinite. Moreover, the claims as presented are at least inherently limited; by common sense if nothing else, to those embodiments that would be useful for detecting an analyte in an sample as recited in the claims. Along these lines, see *In re Anderson*, 176 USPQ 331(CCPA 1973).

Concerning the term three-dimensional array, such term is readily understandable by those skilled in the art and therefore is definite. In fact, the secondary reference relied upon by the Examiner explicitly refers to three-dimensional assemblies (see US patent 6,180,135). Moreover, the Examiner’s statement that a “polydiacetylene backbone” is by its very nature “three-dimensional” and that the claim reads on a “polydiacetylene” in any form including a simple film is contrary to the Restriction Requirement dated January 15, 2001. In the Restriction Requirement, the Examiner explicitly pointed out that the three-dimensional arrays and the two-dimensional arrays are directed to different inventions.

In addition, with respect to the rejections under 35 USC §112, second paragraph, the Examiner’s attention is particularly directed to the following comments by the Court in the case of *In re Goffe*, 191 USPQ 431:

“ for all practical purposes, the Board would limit appellant to claims involving the specific materials disclosed in the Examples, so that a competitor seeking to avoid infringing the claims would merely have to follow the disclosures and the subsequently-issued patent to find a substitute. However, to provide effective incentives, claims must adequately protect inventors. To demand that the first to disclose shall limit his claims to what he has found will work or two materials which meet the guidelines specified for “preferred” materials in a process such as the one herein and involved would not serve the constitutional purpose of promoting progress in the useful arts”.

Moreover, because various terms criticized by the Examiner are somewhat generic does not mean that they are indefinite. Along these lines, the Examiner's attention is kindly directed to *In re Moore*, 169 USPQ 236; *In re Kroekel*, 183 USPQ 610, *In re Miller*, 169 USPQ 597; *Ex parte Kenaga*, 189 USPQ 63; *Ex parte Laiderman*, 175 USPQ 757; *ex parte Schundehutte*, 184 USPQ 697.

Claims 1-19 were rejected under 35 USC 103 (a) as being unpatentable over U.S. 5,415,999 Saul, et al., in view of US patent 6,180,135 B1 to Charych et al. These cited references do not render obvious the present invention. In particular, the claims under consideration relate to detecting an analyte in a sample by contacting the sample to be tested with a three-dimensional array that comprises a polydiacetylene backbone and a substrate wherein the substrate has direct affinity for an analyte or is capable of binding to an analyte or is capable of reacting with an analyte. An analyte when present causes a change in fluorescence of the polydiacetylene backbone. The change in fluorescence is then detected to thereby indicate the presence of an analyte. As discussed in the specification measuring the change in fluorescence of the array is a significantly more sensitive test than monitoring by color change. The increase in sensitivity is crucial for providing detection systems to have actual practical utility as a sensor for many applications where monitoring color change would not be satisfactory.

Moreover, as discussed in the specification, the assay method of the present invention makes possible a continuous monitoring of the binding or the interaction of an analyte. Also, since no wash steps are required in the technique of the present invention, the method is relatively simple and inexpensive to carry out.

U.S. patent 5,415,999 to Saul et al, fails to suggest or render obvious the present invention since, among other things, as recognized by the Examiner, Saul et al., fails to suggest or disclose a three-dimensional array of a polydiacetylene backbone or, according to preferred aspects of the present invention, an array that is in the form of the liposomes or tubules pursuant. Furthermore, Saul et al., fails to suggest the present invention since Saul et al is not concerned with a change in fluorescence of a

polydiacetylene backbone. Instead, Saul et al., requires a red, fluorescent, polydiacetylene film that is layered with fluorescence modulation reagent non-covalently associated with the film. This fluorescence-modulating reagent required by Saul et al., modulates the measured emission of the film, e.g., by absorbing the emitted light, in the response to the presence of an analyte. In other words, the fluorescence state of the film does not change during the assay: rather the emission is obscured or revealed by the action of the fluorescence modulation agent required by Saul et al. Saul et al. does not suggest measuring the change in fluorescence that is due to the interaction or binding of an analyte and the polydiacetylene.

Charych, et al., fails to overcome the above-discussed efficiencies of Saul, et al., with respect to rendering obvious the present invention. In particular Charych, et al., does not relate to using fluorescence but instead relates to a method that monitors color change of a three-dimensional array of a polydiacetylene backbone. Nothing whatsoever in Charych et al., would suggest that the three-dimensional array could be used in a method that detects the change in fluorescence. Furthermore, the three-dimensional arrays suggested by Charych et al., are prepared in the blue form, which is the non-fluorescent form, in order to be suitable for the assays suggested therein. Since the technique suggested by Saul et al., requires starting with a red fluorescent film it would be counterintuitive to employ the non-fluorescent three-dimensional array suggested by Charych et al., in the method of Saul et al. Accordingly, the prior art lacks any motivation to substitute the polydiacetylene three-dimensional arrays employed by Charych et al., in the method of Saul et al. In fact, if anything, the cited art actually leads from the present invention.

Furthermore, even if such were substituted in the method of Saul et al., the present invention would still not be suggested since, as discussed above, Saul et al., require a fluorescent modulating reagent which obscures or reveals the fluorescence of emissions of the film.

In addition, the Examiner's statement that criticality has not been demonstrating for the use of fluorescence rather than colorimetric polydiacetylene backbone is not germane to this matter, since the Examiner has not even established a *prima facie* case of obviousness. When the proposed modification would change the principle of operation of the prior art being modified, as is the case here, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. See *In re Ratti* 123 USPQ 349 (CCPA 1959). Furthermore, as discussed in the specification, fluorescence in colorimetric techniques is not the same and fluorescence clearly provides a more sensitive technique.

In addition, Claim 9 which is directed to that aspect of the present invention wherein the polydiacetylene is in the non-fluorescent form is non-obvious since Saul et al., requires a polydiacetylene film that is in the fluorescent form to be suitable for the technique suggested therein. Accordingly, use of a non-fluorescent form would not be suitable for the express purposes of Saul et al.

The mere fact that cited art may be modified in the manner suggested by the Examiner does not make this modification obvious, unless the cited art suggest the desirability of the modification. No such suggestion appears in the cited art in this matter. The Examiner's attention is kindly directed to *In re Lee* 61 USPQ 2d 1430 (Fed. Cir. 2002) *In re Dembiczak et al.* 50 USPQ2d. 1614 (Fed. Cir. 1999), *In re Gordon*, 221 USPQ 1125 (Fed. Cir. 1984), *In re Laskowski*, 10 USPQ2d. 1397 (Fed. Cir. 1989) and *In re Fritch*, 23, USPQ2d. 1780 (Fed. Cir. 1992).

In *Dembiczak et al.*, supra, the Court at 1617 stated: "Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references. See, e.g., *C.R. Bard, Inc., v. M3 Sys., Inc.*, 157 F.3d. 1340, 1352, 48 USPQ2d. 1225, 1232 (Fed. Cir. 1998) (describing 'teaching or suggestion motivation [to combine]' as in 'essential evidentiary component of an obviousness holding'), *In re Rouffet*, 149 F.3d 1350, 1359, 47 USPQ2d. 1453, 1459

(Fed. Cir. 1998) ('the Board must identify specifically...the reasons one of ordinary skill in the art would have been motivated to select the references and combine them');...".

Also, the cited art lacks the necessary direction or incentive to those of ordinary skill in the art to render under 35 USC 103 sustainable. The cited art fails to provide the degree of predictability of success of achieving the properties attainable by the present invention needed to sustain a rejection under 35 USC 103. See *Diversitech Corp. v. Century Steps, Inc.* 7 USPQ2d 1315 (Fed. Cir. 1988), *In re Mercier*, 185 USPQ 774 (CCPA 1975) and *In re Naylor*, 152 USPQ 106 (CCPA 1966).

Moreover, the properties of the subject matter and improvements which are inherent in the claimed subject matter and disclosed in the specification are to be considered when evaluating the question of obviousness under 35 USC 103. See *Gillette Co. v. S.C. Johnson & Son, Inc.*, 16 USPQ2d. 1923 (Fed. Cir. 1990), *In re Antonie*, 195, USPQ 6 (CCPA 1977), *In re Estes*, 164 USPQ (CCPA 1970), and *In re Papesch*, 137 USPQ 43 (CCPA 1963).

No property can be ignored in determining patentability and comparing the claimed invention to the cited art. Along these lines, see *In re Papesch*, supra, *In re Burt et al*, 148 USPQ 548 (CCPA 1966), *In re Ward*, 141 USPQ 227 (CCPA 1964), and *In re Cescon*, 177 USPQ 264 (CCPA 1973).

In view of the above, consideration and allowance are, therefore, respectfully solicited.

In the event the Examiner believes an interview might serve to advance the prosecution of this application in any way, the undersigned attorney is available at the telephone number noted below.

The Director is hereby authorized to charge any fees, or credit any overpayment, associated with this communication, including any extension fees, to CBLH Deposit Account No. 22-0185.

Respectfully submitted,



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